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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,276	03/07/2001	John W. Erickson	207596	9981

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,276	ERICKSON ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47 and 49-66* is/are pending in the application.

4a) Of the above claim(s) *1-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47, and 49-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *05* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648, Emily Le.

Status of Claims

2. Claims 1-47 and 49-66 are pending. Claim 48 has been canceled. Claims 1-46 are non-elected claims, thus, are withdrawn from examination. Claims 47 and 49-66 are currently under examination.

3. Applicant's election with traverse of a method of preventing the development of drug resistance in Paper No. 07 is acknowledged. The traversal is on the ground(s) that the analysis provided in the previous office action is limited to comparing Groups II-VII to Group I. Moreover, the designation of Groups III and IV is inconsistent with the species requirement of Groups I and II; specifically the species election distinguishes a retrovirus, whereas Group III is directed to using the invention of Group I for HIV, a retrovirus. The same argument was also applied to Groups II and IV. Further, Applicant argues that the search for Group VI would be overlapping for Group VII because the two Groups share a common technical feature.

The argument presented by Applicant in Paper No. 7 has been found persuasive, Thus, Groups I and III, Groups II and IV, and Groups VI and VII are now rejoined. Groups III, IV, and VII are no longer in existence. Group III is now rejoined to Group I

under sub-group III. Further, sub-group III of Groups I and II is rejoined with sub-group II of Groups I and II. Thus, sub-group III of Groups I and II is no longer in existence.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: detailed information such as inventor's signature, country of citizenship, residence, and postal address is missing for the third inventor, Mitsuya Hiroaki.

Information Disclosure Statement

5. The information disclosure statement (IDS) filed 05/26/01 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Applicant did not provide a copy of most non-patent literature and some foreign patents documents at the time of submission of the IDS.

6. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate

paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

7. The information disclosure statement filed 05/26/01, specifically WO 90/09191 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

8. Claims 63-66 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims are directed toward a method of treating a mutant retroviral infection in a mammal infected with a mutant retrovirus, which method comprises administering to said mammal a mutant retroviral-inhibiting effective amount of a compound or composition defined by claim 47. Claim 47 is a method claim, not a compound or a composition claim. Thus, claims 63-66 are deemed to be of improper dependent form for failing to further limit claim 47.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 47-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the composition/compound that is used in the method claims, does not reasonably provide enablement for a method of preventing the development of drug resistance in an HIV infected mammal or to treat a mutant retroviral infection in a mammal infected with a mutant retrovirus with the administration of a drug resistance-inhibiting compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/use the invention commensurate in scope with these claims.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

The nature of the invention is a method to prevent the development of drug resistance in an HIV-infected mammal or to treat a mutant retroviral infection in a mammal infected with a mutant retrovirus with the administration of a compound.

The state of the art is such that it is well known that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to therapy of HIV are well documented in the literature. These obstacles include: 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein; 2) the fact that the modes of viral transmission include both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission; 3) the existence of a latent form of the virus; 4) the ability of the virus to evade immune responses in the central nervous system due to the blood-brain barrier; and 5) the complexity and variation of the pathology of HIV infection in different

individuals. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation. The quantity of experimentation necessary is generally high. The claims are directed toward a method of preventing the development of drug resistance in an HIV infected mammal or to treat a mutant retroviral infection in a mammal infected with a mutant retrovirus with the administration of a drug resistance-inhibiting compound. The administration of the compound in a mammal implies that claimed method involves an *in vivo* use of the compounds to prevent the development of drug resistance in an HIV infected mammal or to treat a mutant retroviral infection in a mammal infected with a mutant retrovirus. The specification does not provide any evidence of *in vivo* use nor has the specification provided any data that supports that the claimed method is effective in preventing the development of drug resistance in an HIV-infected mammal or to treat a mutant retroviral infection in a mammal infected with a mutant retrovirus.

Further, as taught by Fahey et al., clinical trials using a variety of immunologically based therapies have not yielded successful results in the treatment and/or prevention of HIV infection. Fox further discusses the failure of all immune-system-boosting therapies for treating AIDS. Thus, it is clear from the evidence of Fahey et al. and Fox, that the ability to treat and/or prevent HIV infection is highly unpredictable and has met with very little success. Applicants have not provided any convincing evidence that their method is indeed useful to prevent the development of drug resistance in an HIV-infected mammal or to treat a mutant retroviral infection in a

mammal infected with a mutant retrovirus with the administration of a drug resistant-inhibiting compound. The evidences provided in the specification are not enabling to the claimed invention because most of the examples are directed to an *in vitro* use of the claimed invention with the exception of one example. The exception relates to an *in vivo* use of the compound used in the claimed method in rats to demonstrate oral absorption of the compound. This sole *in vivo* study is not enabling for the prevention of the development of drug resistance in an HIV-infected mammal or treatment a mutant retroviral infection in a mammal infected with a mutant retrovirus. The example lacks correlation or data that connects the claimed invention with the oral absorption data. Further, *in vitro* studies that demonstrate a compound's effectiveness in preventing the development of drug resistance in an HIV-infected mammal or in treating a mutant retroviral infection in a mammal infected with a mutant retrovirus does not means that the same compound would have similar effect *in vivo*, as exemplified by L-735,524, Merck's trade designation for their drug resistant compound. Merck's observed that there was no drug resistance to L-735,524 in cell culture studies prior to human trials, however, data gathered from clinical evaluations has indicated otherwise (Waldholz).

Lastly, Applicant has not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. The amount of direction or guidance presented the specification is sparse. The specification does not taught how to make and/or use the composition to effectively prevent the development of drug resistance in an HIV-infected mammal or to treat a mutant retroviral infection in a mammal infected with a mutant

retrovirus nor has the specification provided sufficient detail on the mode of administration, duration of treatment, and the effective amount to administer to mammals that are evident to be HIV drug resistant or infected with a mutant retrovirus.

In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (703) 305-4452. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0169.

E.Le

JAMES HOUSEL 11/3/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600